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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/670,490 | 09/25/2003 | Eytan R. Barnea | 120785.0310 | 8761 |
| 7590 04/07/2008 | | | | |
| Pepper Hamilton LLP Firm 21269 500 Grant Street One Mellon Center, 50th Floor Pittsburgh, PA 15219 | | | EXAMINER | |
| | | | CANELLA, KAREN A | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1643 | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/670,490

Applicant(s)

BARNEA ET AL

Examiner

Karen A. Canella

Art Unit

1643

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 9-22 and 25-30 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 9-22 and 25-30 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SE/US)
Paper No(s)/Mail Date ____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date ____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: ____.

DETAILED ACTION

Claims 9, 15, and 25-29 have been amended. Claims 9-22 and 25-30 are pending and under consideration.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-22 and 25-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention..

(A) As drawn to peptides without anti-proliferative activity

The instant specification states that the mixture of peptides corresponding to SEQ ID NO:1-12 possessed no inhibitory activity against MCF-7 cells, but that SEQ ID NO:2, 3 and 8 possessed significant inhibitory activity, and explains that the remainder of the peptides are able to compete with the active peptides for receptor sites on MCF-7, but do not possess inhibitory activity (page 26, line 22 to page 27, line 13). The specification further teaches that out of the peptides A-M, that A, F and K exhibited significant anti-proliferative activity but that "other peptides were less activity or showed no activity" (page 27, lines 6-8). Thus the specification admits that some of the peptides A-M, outside of the peptides of A, F and K, exhibit no anti-proliferative activity. Applicant argues that the anti-proliferative activity is demonstrated in Figure 9. This is not persuasive. Figure 9 indicates that B and C have nearly the same proliferative activity as the negative control. There is no indication of the statistical significance for the relative numbers for proliferation between the negative control and the B plus C peptides. In light of the specification admitting that some of the peptides show no anti-proliferative activity, and the lack of teachings regarding the statistical similarity or difference between the anti-proliferative activity of peptides B combined with C relative to the negative control, it would be reasonable to conclude that peptides B and C have no anti-proliferative activity. One

of skill in the art would be subject to undue experimentation in order to use the products of claims 22, 25 and 30 with peptides other than SEQ ID NO:2, 3 or 8 because the specification fails to provide an alternative use for a peptide which is not an anti-proliferative peptide. One of skill in the art would also be subject to undue experimentation in order to use the peptides corresponding to the peptides of B and C which would include peptides of SEQ ID NO:1, 4-7 and/or 9-12 because said peptides would not be expected to have anti-proliferative activity.

(B) As drawn to the administration of the peptides to inhibit a viral infection or cancer in a patient.

Claims 15-21 and 27 are drawn to methods of inhibiting viral proliferation in a subject. The specification teaches that the anti-proliferative ability of the low molecular weight peptides was quantitated using an MCF7 breast cancer cell line. This fails to provide any nexus with a method of treatment of a subject having a viral infection. The specification fails to teach a molecular nexus between the inhibition of growth of a breast cancer cell line and the inhibition of a viral infection. The specification fails to provide an objective evidence that the administration of the instant peptides can inhibit a viral infection or any viral infection, in a subject. The art recognizes that many compounds can show favorable activity in vitro but fail to show favorable activity in a clinical treatment. Mohanlal (WO0240717) teaches that an important reason for the high failure rate in clinical trials is the poor predictive value of currently used screening technologies for biological validation, pharmacological testing, and screening for success or failure of chemical entities and biologicals in clinical trials involving human subjects, which include screening based on in vitro assays, which inadequately represent the clinical disease phenotype of the patients in which the tested chemical entities or biologicals are intended to be used in the future. Mohanlal teaches that success of chemical entities or biologicals in cell screens does not necessarily translate into clinical success in patients because the majority of chemical entities or biologicals, while successful in said cell screens fail in clinical trials, particularly in late phase II and phase III trials for pharmacodynamic reasons (lack of efficacy and/or an unacceptable adverse event profile); and pharmacokinetic reasons.

Applicant argues that it is not necessary to provide results in an animal model in order to demonstrate enablement. This has been considered but not found persuasive. The inhibition of pathological cells in vivo is complex and the art is unreliable. The MPEP (2163.03) states:

...in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. In re Soll, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991).

It is noted that “physiological activity” is classified as unpredictable which corroborates the teachings of Mohanlal (WO0240717) on the poor predictive value of currently used screening technologies for biological validation, pharmacological testing, include screening based on in vitro assays, which inadequately represent the clinical disease phenotype of the patients. It is further noted that there is no objective evidence in the art that agents which inhibit the proliferation of cancer cells, such as doxorubicin and etoposide would also inhibit proliferation of viral infection in a subject. Conversely, agents such as anti-retrovirals, do not inhibit the proliferation of cancer cells in a subject. Thus, there appears to be no molecular basis for extending the observation that peptides of SEQ ID NO:2, 3, and 8 inhibit the growth of a breast cancer cell line in vitro to the inhibition of a viral infection in a subject.

All other rejections and objections as set forth or maintained in the prior Office action are withdrawn in light of applicants amendments.

All claims are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

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MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A Canella/

Primary Examiner, Art Unit 1643